WHAT IS CLAIMED IS:

1. A method for purifying double-stranded polynucleotides lacking base pair mismatches, insertion/deletion loops and/or a nucleotide gap or gaps comprising the following steps:

(a) providing a plurality of polypeptides that specifically bind to a base pair mismatch, an insertion/deletion loop and/or a nucleotide gap or gaps within a double stranded polynucleotide;

(b) providing a sample comprising a plurality of double-stranded polynucleotides;

(c) contacting the double-stranded polynucleotides of step (b) with the polypeptides of step (a) under conditions wherein a polypeptide of step (a) can specifically bind to a base pair mismatch, an insertion/deletion loop and/or a nucleotide gap or gaps in a double stranded polynucleotide of step (b); and

(d) separating the double-stranded polynucleotides lacking a specifically bound polypeptide of step (a) from the double-stranded polynucleotides to which a polypeptide of step (a) has specifically bound, thereby purifying double-stranded polynucleotides lacking base pair mismatches, insertion/deletion loops and/or a nucleotide gap or gaps.

2. The method of claim 1, wherein the double-stranded polynucleotide comprises a double-stranded oligonucleotide.

3. The method of claim 1, wherein the double-stranded polynucleotide is between 3 and about 300 base pairs in length.

4. The method of claim 3, wherein the double-stranded polynucleotide is between 10 and about 200 base pairs in length.

5. The method of claim 4, wherein the double-stranded polynucleotide is between 50 and about 150 base pairs in length.

6. The method of claim 1, wherein the base pair mismatch comprises a C:T mismatch.

7. The method of claim 1, wherein the base pair mismatch comprises a G:A mismatch.

8. The method of claim 1, wherein the base pair mismatch comprises a C:A mismatch.

9. The method of claim 1, wherein the base pair mismatch comprises a G:U/T mismatch.

10. The method of claim 1, wherein a polypeptide that specifically binds to a base pair mismatch, an insertion/deletion loop or a nucleotide gap within a double stranded polynucleotide comprises a DNA repair enzyme.

11. The method of claim 10, wherein the DNA repair enzyme is a bacterial DNA repair enzyme.

12. The method of claim 11, wherein the bacterial DNA repair enzyme comprises a MutS DNA repair enzyme.

13. The method of claim 12, wherein the MutS DNA repair enzyme comprises a Taq MutS DNA repair enzyme.

14. The method of claim 11, wherein the bacterial DNA repair enzyme comprises an Fpg DNA repair enzyme.

15. The method of claim 11, wherein the bacterial DNA repair enzyme comprises a MutY DNA repair enzyme.

16. The method of claim 11, wherein the bacterial DNA repair enzyme comprises a hexA DNA mismatch repair enzyme.

17. The method of claim 11, wherein the bacterial DNA repair enzyme comprises a Vsr mismatch repair enzyme.

18. The method of claim 10, wherein the DNA repair enzyme is a mammalian DNA repair enzyme.

19. The method of claim 10, wherein the DNA repair enzyme is a DNA glycosylase that initiates base-excision repair of G:U/T mismatches.

20. The method of claim 19, wherein the DNA glycosylase comprises a bacterial mismatch-specific uracil-DNA glycosylase (MUG) DNA repair enzyme.

21. The method of claim 19, wherein the DNA glycosylase comprises a eukaryotic thymine-DNA glycosylase (TDG) enzyme.

22. The method of claim 1, wherein the polypeptide that specifically binds to a base pair mismatch, an insertion/deletion loop or a nucleotide gap further comprises a biotin molecule.

23. The method of claim 1, wherein the polypeptide that specifically binds to a base pair mismatch, an insertion/deletion loop or a nucleotide gap further comprises a molecule comprising an epitope capable of being specifically bound by an antibody.

24. The method of claim 1, wherein the insertion/deletion loop comprises a stem-loop structure.

25. The method of claim 1, wherein the insertion/deletion loop comprises a single base pair mismatch.

26. The method of claim 25, wherein the insertion/deletion loop comprises two consecutive base pair mismatches.

27. The method of claim 26, wherein the insertion/deletion loop comprises three consecutive base pair mismatches.

28. The method of claim 1, wherein the separating of the double-stranded polynucleotides lacking a specifically bound polypeptide of step (a) from the double-stranded polynucleotides to which a polypeptide of step (a) has specifically bound of step (d) comprises use of an antibody, wherein the antibody is capable of specifically binding to the specifically bound polypeptide or an epitope bound to the specifically bound polypeptide and the antibody is contacted with the specifically bound polypeptide under conditions wherein the antibodies are capable of specifically binding to the specifically bound polypeptide or an epitope bound to the specifically bound polypeptide.

29. The method of claim 28, wherein the antibody is an immobilized antibody.

30. The method of claim 29, wherein the antibody is immobilized onto a bead or a magnetized particle.

31. The method of claim 30, wherein the antibody is immobilized onto a magnetized bead.

32. The method of claim 29, wherein the antibody is an immobilized in an immunoaffinity column and the sample is passed through the immunoaffinity column under conditions wherein the immobilized antibodies are capable of specifically binding to the specifically bound polypeptide or the epitope bound to the specifically bound polypeptide.

33. The method of claim 1, wherein the separating of the double-stranded polynucleotides lacking a specifically bound polypeptide of step (a) from the double-stranded polynucleotides to which a polypeptide of step (a) has specifically bound of step (d) comprises use of an affinity column, wherein the column comprises immobilized binding molecules capable of specifically binding to a tag linked to the specifically bound polypeptide and the sample is passed through the affinity column under conditions wherein the immobilized antibodies are capable of specifically binding to the tag linked to the specifically bound polypeptide.

34. The method of claim 33, wherein the immobilized binding molecules comprise an avidin and the tag linked to the specifically bound polypeptide comprises a biotin.

35. The method of claim 1, wherein the separating of the double-stranded polynucleotides lacking a specifically bound polypeptide of step (a) from the double-stranded polynucleotides to which a polypeptide of step (a) has specifically bound of step (d) comprises use of a size exclusion column.

36. The method of claim 35, wherein the size exclusion column comprises a spin column.

37. The method of claim 1, wherein the separating of the double-stranded polynucleotides lacking a specifically bound polypeptide of step (a) from the double-stranded polynucleotides to which a polypeptide of step (a) has specifically bound of step (d) comprises use of a size exclusion gel.

38. The method of claim 37, wherein the size exclusion gel comprises an agarose gel.

39. The method of claim 1, wherein the double-stranded polynucleotide comprises a polypeptide coding sequence.

40. The method of claim 39, wherein the polypeptide coding sequence comprises a fusion protein coding sequence.

41. The method of claim 40, wherein the fusion protein comprises a polypeptide of interest upstream to an intein, wherein the intein encodes a polypeptide.

42. The method of claim 41, wherein the intein polypeptide comprises an antibody or ligand.

43. The method of claim 41, wherein the intein polypeptide comprises an enzyme.

44. The method of claim 43, wherein the enzyme comprises Lac Z.

45. The method of claim 43, wherein the intein polypeptide comprises a polypeptide selectable marker.

46. The method of claim 45, wherein the polypeptide selectable marker comprises an antibiotic.

47. The method of claim 46, wherein the antibiotic comprises a kanamycin, a penicillin or a hygromycin.

48. A method for assembling double-stranded oligonucleotides to generate a polynucleotide lacking base pair mismatches, insertion/deletion loops and/or a nucleotide gap or gaps comprising the following steps:

(a) providing a plurality of polypeptides that specifically bind to a base pair mismatch, an insertion/deletion loop and/or a nucleotide gap or gaps in a double stranded polynucleotide;

(b) providing a sample comprising a plurality of double-stranded oligonucleotides;

(c) contacting the double-stranded oligonucleotides of step (b) with the polypeptides of step (a) under conditions wherein a polypeptide of step (a) can specifically bind to a base pair mismatch, an insertion/deletion loop and/or a nucleotide gap or gaps in a double stranded oligonucleotide of step (b);

(d) separating the double-stranded oligonucleotides lacking a specifically bound polypeptide of step (a) from the double-stranded oligonucleotides to which a polypeptide of step (a) has specifically bound, thereby purifying double-stranded oligonucleotides lacking base pair mismatches, insertion/deletion loops and/or a nucleotide gaps; and

(e) joining together the purified double-stranded oligonucleotides lacking base pair mismatches, insertion/deletion loops and/or a nucleotide gaps, thereby generating a polynucleotide lacking base pair mismatches, insertion/deletion loops and/or a nucleotide gap or gaps.

49. The method of claim 48, wherein the oligonucleotides comprise a library of oligonucleotides.

50. The method of claim 49, wherein the oligonucleotides comprise a library of double-stranded oligonucleotides.

51. The method of claim 49, wherein the library of oligonucleotides multicodon building blocks, the library comprises a plurality of double-stranded oligonucleotide members, wherein each oligonucleotide member comprises at least two codons in tandem and a Type-IIS restriction endonuclease recognition sequence flanking the 5' and the 3' end of the multicodon.

52. A method for generating a polynucleotide lacking base pair mismatches, insertion/deletion loops and/or a nucleotide gap or gaps comprising the following steps:

(a) providing a plurality of polypeptides that specifically bind to a base pair mismatch, an insertion/deletion loop and/or a nucleotide gap or gaps in a double stranded polynucleotide;

(b) providing a sample comprising a plurality of double-stranded oligonucleotides;

(c) joining together the double-stranded oligonucleotides of step (b) to generate a double-stranded polynucleotide;

(d) contacting the double-stranded polynucleotide of step (c) with the polypeptides of step (a) under conditions wherein a polypeptide of step (a) can specifically bind to a base pair mismatch, an insertion/deletion loop and/or a nucleotide gap or gaps in a double stranded polynucleotide of step (c); and

(e) separating the double-stranded polynucleotides lacking a specifically bound polypeptide of step (a) from the double-stranded polynucleotides to which a polypeptide of step (a) has specifically bound, thereby purifying double-stranded polynucleotides lacking base pair mismatches, insertion/deletion loops and/or a nucleotide gap or gaps.

53. The method of claim 52, wherein the double-stranded oligonucleotides comprise a library of oligonucleotides multicodon building blocks, the library comprising a plurality of double-stranded oligonucleotide members, wherein each oligonucleotide member comprises at least two codons in tandem and a Type-IIS restriction endonuclease recognition sequence flanking the 5' and the 3' end of the multicodon.

54. The method of claim 53, further comprising providing a set of 61 immobilized starter oligonucleotides, one oligonucleotide for each possible amino acid coding triplet, wherein the oligonucleotides are immobilized on a substrate and have a single-stranded overhang corresponding to a single-stranded overhang generated by a Type-IIS restriction endonuclease, or, the oligonucleotides comprise a Type-IIS restriction endonuclease recognition site distal to the substrate and a single-stranded overhang is generated by digestion with a Type-IIS restriction endonuclease; digesting a second oligonucleotide member from the library of step (a) with a Type-IIS restriction endonuclease

to generate a single-stranded overhang; and contacting the digested second oligonucleotide member to the immobilized first oligonucleotide member under conditions wherein complementary single-stranded base overhangs of the first and the second oligonucleotides can pair, and, ligating the second oligonucleotide to the first oligonucleotide, thereby generating a double-stranded polynucleotide.

55. A method for generating a base pair mismatch-free, an insertion/ deletion loop-free and/or a nucleotide gap-free double-stranded polypeptide coding sequence comprising the following steps:

(a) providing a plurality of polypeptides that specifically bind to a base pair mismatch, an insertion/deletion loop and/or a nucleotide gap or gaps within a double stranded polynucleotide;

(b) providing a sample comprising a plurality of double-stranded polynucleotides encoding a fusion protein, wherein the fusion protein coding sequence comprises a coding sequence for a polypeptide of interest upstream of and in frame with a coding sequence for a marker or a selection polypeptide;

(c) contacting the double-stranded polynucleotides of step (b) with the polypeptides of step (a) under conditions wherein a polypeptide of step (a) can specifically bind to a base pair mismatch, an insertion/deletion loop and/or a nucleotide gap or gaps in a double stranded polynucleotide of step (b);

(d) separating the double-stranded polynucleotides lacking a specifically bound polypeptide of step (a) from the double-stranded polynucleotides to which a polypeptide of step (a) has specifically bound, thereby purifying double-stranded polynucleotides lacking base pair mismatches, insertion/deletion loops and/or a nucleotide gaps;

(e) expressing the purified double-stranded polynucleotides and selecting the polynucleotides expressing the selection marker polypeptide, thereby generating a base pair mismatch-free, an insertion/ deletion loop-free and/or a nucleotide gap-free polypeptide coding sequence.

56. The method of claim 55, wherein the marker or selection polypeptide comprises a self-splicing intein, and the method further comprises the self-splicing out of the marker or selection polypeptide from the upstream polypeptide of interest.

57. The method of claim 55, wherein the marker or selection polypeptide comprises an enzyme.

58. The method of claim 57, wherein the enzyme comprises a Lac Z.

59. The method of claim 58, wherein the marker or selection polypeptide comprises an antibiotic.

60. The method of claim 59, wherein the antibiotic comprises a kanamycin, a penicillin or a hygromycin.

61. The method of claim 1, wherein the purified double-stranded polynucleotides are 95% free of base pair mismatches, insertion/deletion loops and/or nucleotide gaps.

62. The method of claim 61, wherein the purified double-stranded polynucleotides are 98% free of base pair mismatches, insertion/deletion loops and/or nucleotide gaps.

63. The method of claim 62, wherein the purified double-stranded polynucleotides are 99% free of base pair mismatches, insertion/deletion loops and/or nucleotide gaps.

64. The method of claim 63, wherein the purified double-stranded polynucleotides are completely free of base pair mismatches, insertion/deletion loops and/or nucleotide gaps.

65. The method of claim 1, wherein the method comprises purifying polynucleotides that have been manipulated by a method comprising gene site saturated mutagenesis (GSSM).

66. The method of claim 1, wherein the method comprises purifying polynucleotides that have been manipulated by a method comprising synthetic ligation reassembly (SLR).

67. The method of claim 1, wherein the method comprises purifying polynucleotides that have been manipulated by a method selected from the group consisting of gene site saturated mutagenesis (GSSM), step-wise nucleic acid reassembly, error-prone PCR, shuffling, oligonucleotide-directed mutagenesis, assembly PCR, sexual PCR mutagenesis, in vivo mutagenesis, cassette mutagenesis, recursive ensemble mutagenesis, exponential ensemble mutagenesis, site-specific mutagenesis, gene reassembly, synthetic ligation reassembly (SLR) and a combination thereof.

68. The method of claim 1, wherein the method comprises purifying polynucleotides that have been manipulated by a method selected from the group consisting of recombination, recursive sequence recombination, phosphothioate-modified DNA mutagenesis, uracil-containing template mutagenesis, gapped duplex mutagenesis, point mismatch repair mutagenesis, repair-deficient host strain mutagenesis, chemical mutagenesis, radiogenic mutagenesis, deletion mutagenesis, restriction-selection mutagenesis, restriction-purification mutagenesis, artificial gene synthesis, ensemble mutagenesis, chimeric nucleic acid multimer creation and a combination thereof.

69. The method of claim 1, wherein the method comprises purifying a double-stranded nucleic acid comprising a synthetic polynucleotide.

70. The method of claim 69, wherein the synthetic polynucleotide is identical to a parental or natural sequence.

71. The method of claim 1, wherein the method comprises purifying a double-stranded nucleic acid comprising a synthetic polynucleotide, a recombinantly generated nucleic acid or an isolated nucleic acid.

72. The method of claim 71, wherein the polynucleotide comprises a gene.

73. The method of claim 72, wherein the polynucleotide comprises a chromosome.

74. The method of claim 72, wherein the gene further comprises a pathway.

75. The method of claim 72, wherein the gene comprises a regulatory sequence.

76. The method of claim 75, wherein the regulatory sequence comprises a promoter or an enhancer.

77. The method of claim 71, wherein the polynucleotide comprises a polypeptide coding sequence.

78. The method of claim 77, wherein the polypeptide is an enzyme, an antibody, a receptor, a neuropeptide, a chemokine, a hormone, a signal sequence, or a structural gene.

79. The method of claim 71, wherein the polynucleotide comprises a non-coding sequence.

80. The method of claim 1, wherein the polynucleotide comprises a DNA, an RNA or a combination thereof.

81. The method of claim 80, wherein a sample or "batch" of double-stranded DNA or RNA is generated that is 90%, 95%, 96%, 97%, 98%, 99%, 99.5% or 100% or completely free of base pair mismatches, insertion/deletion loops and/or a nucleotide gap or gaps.

82. The method of claim 1, wherein the double-stranded polynucleotide comprises an iRNA.

83. The method of claim 1, wherein the double-stranded polynucleotide comprises a DNA.

84. The method of claim 83, wherein the DNA comprises a gene.

85. The method of claim 84, wherein the DNA comprises a chromosome.

86. A library of oligonucleotides comprising dicodon building blocks, the library comprising a plurality of double-stranded oligonucleotide members, wherein each oligonucleotide member comprises two codons in tandem (a dicodon) and a Type-IIS restriction endonuclease recognition sequence flanking the 5' and the 3' end of the dicodon.

87. The library of claim 86, wherein the library comprises oligonucleotide members comprising all possible codon dimer (dicodon) combinations.

88. The library of claim 86, wherein the oligonucleotide members comprise 4096 possible codon dimer (dicodon) combinations.

89. The library of claim 86, wherein the codons code for a promoter, an enhancer, a regulatory motif non-coding sequence, a telomere or a structural non-coding sequence.

90. The library of claim 86, wherein the Type-IIS restriction endonuclease recognition sequence at the 5' end of the dicodon differs from the Type-IIS restriction endonuclease recognition sequence at the 3' end of the dicodon.

91. The library of claim 86, wherein the Type-IIS restriction endonuclease recognition sequence is specific for a restriction endonuclease that, upon digestion of the oligonucleotide library member, generates a three base single-stranded overhang.

92. The library of claim 91, wherein the restriction endonuclease comprises a SapI restriction endonuclease or an isochizomer thereof.

93. The library of claim 91, wherein the restriction endonuclease comprises an EarI restriction endonuclease or an isochizomer thereof.

94. The library of claim 86, wherein the Type-IIS restriction endonuclease recognition sequence is specific for a restriction endonuclease that, upon digestion of the oligonucleotide library member, generates a two base single-stranded overhang.

95. The library of claim 94, wherein the restriction endonuclease is selected from the group consisting of BseRI, BsgI and BpmI.

96. The library of claim 86, wherein the Type-IIS restriction endonuclease recognition sequence is specific for a restriction endonuclease that, upon digestion of the oligonucleotide library member, generates a one base single-stranded overhang.

97. The library of claim 96, wherein the restriction endonuclease is selected from the group consisting of N.AlwI and N.BstNBI.

98. The library of claim 86, wherein the Type-IIS restriction endonuclease recognition sequence is specific for a restriction endonuclease that, upon digestion of the

oligonucleotide library member, cuts on both sides of the Type-IIS restriction endonuclease recognition sequence.

99. The library of claim 98, wherein the restriction endonuclease is selected from the group consisting of BcgI, BsaXI and BspCNI.

100. The library of claim 86, wherein each oligonucleotide library member consists essentially of two codons in tandem (a dicodon) and a Type-IIS restriction endonuclease recognition sequence flanking the 5' and the 3' end of the dicodon.

101. The library of claim 86, wherein the oligonucleotide library members are between about 20 and 400 base pairs in length.

102. The library of claim 101, wherein the oligonucleotide library members are between about 40 and 200 base pairs in length.

103. The library of claim 102, wherein the oligonucleotide library members are between about 100 and 150 base pairs in length.

104. The library of claim 86, wherein an oligonucleotide library member comprises a sequence

(NNN)(NNN) AGAAGAGC (SEQ ID NO:1)

(NNN)(NNN) TCTTCTCG (SEQ ID NO:2)

wherein (NNN) is a codon and N is A, C, T or G or an equivalent thereof.

105. The library of claim 86, wherein an oligonucleotide library member comprises a sequence

(NNN)(NNN) TGAAGAGAG (SEQ ID NO:3)

(NNN)(NNN) ACTTCTCTC (SEQ ID NO:4)

wherein (NNN) is a codon and N is A, C, T or G or an equivalent thereof.

106. The library of claim 86, wherein an oligonucleotide library member comprises a sequence

(NNN)(NNN) TGAAGAGAG CT GCTACTAACT GCA (SEQ ID NO:5)

(NNN)(NNN) ACTTCTCTC GA CGATGATTG (SEQ ID NO:6)

wherein (NNN) is a codon and N is A, C, T or G or an equivalent thereof.

107. The library of claim 86, wherein an oligonucleotide library member comprises a sequence

CTCTCTTCA NNN NNN AGAAGAGC (SEQ ID NO:7)

GAGAGAAGT NNN NNN TCTTCTCG (SEQ ID NO:8)

wherein (NNN) is a codon and N is A, C, T or G or an equivalent thereof.

108. The library of claim 86, wherein an oligonucleotide library member comprises a sequence

CTCTCTTCA NNN NNN AGAAGAGC GGGTCTTCCAACTAGAGAATTCGATATCTGCA (SEQ ID NO:9)

GAGAGAAGT NNN NNN TCTTCTCG CCCAGAAGGTTGATCTCTTAAGCTATAG (SEQ ID NO:10)

wherein (NNN) is a codon and N is A, C, T or G or an equivalent thereof.

109. A method for building a polynucleotide comprising codons by iterative assembly of dicodon building blocks, the method comprising the following steps:

(a) providing a library of codon building block oligonucleotides as set forth in claim 1;

(b) providing a substrate surface;

(c) immobilizing a first oligonucleotide member from the library of step (a) to the substrate surface of step (b) and digesting with a Type-IIS restriction endonuclease to generate a single-stranded overhang in a codon, or, digesting a first oligonucleotide member from the library of step (a) with a Type-IIS restriction endonuclease to generate a single-stranded overhang in a codon and immobilizing to the substrate surface of step (b) by the oligonucleotide end opposite the codon;

(d) digesting a second oligonucleotide member from the library of step (a) with a Type-IIS restriction endonuclease to generate a single-stranded overhang in a codon; and

(e) contacting the digested second oligonucleotide member of step (d) to the digested immobilized first oligonucleotide member of step (c) under conditions wherein complementary single-stranded base overhangs of the first and the second oligonucleotides can pair, and, ligating the second oligonucleotide to the first oligonucleotide; thereby building a polynucleotide comprising codons by iterative assembly of dicodon building blocks.

110. The method of claim 109, further comprising digesting the immobilized oligonucleotide of step (e) with a Type-IIS restriction endonuclease to generate a single-stranded overhang in a codon, wherein the Type-IIS restriction endonuclease recognizes a restriction endonuclease recognition sequence in the oligonucleotide distal to the substrate surface.

111. The method of claim 110, further comprising digesting another oligonucleotide member from the library of step (a) with a Type-IIS restriction endonuclease to generate a single-stranded overhang in a codon.

112. The method of claim 110, further comprising contacting a digested oligonucleotide library member to a digested immobilized first oligonucleotide member under conditions wherein complementary single-stranded base overhangs of the oligonucleotides can pair, and, ligating the oligonucleotides; thereby building a polynucleotide comprising codons by iterative assembly of dicodon building blocks.

113. The method of claim 109, wherein the method is repeated iteratively, thereby building a polynucleotide comprising codons.

114. The method of claim 113, wherein the method is iteratively repeated n times, wherein n is an integer between 2 and 10^6.

115. The method of claim 114, wherein the method is iteratively repeated n times, wherein n is an integer between 10^2 and 10^5.

116. The method of claim 109, wherein a member of the library is randomly selected for iterative assembly.

117. The method of claim 116, wherein all the members of the library are selected randomly.

118. The method of claim 109, wherein a member of the library is non-stochastically selected for iterative assembly.

119. The method of claim 118, wherein all the members of the library are selected non-stochastically.

120. The method of claim 109, wherein the library of oligonucleotides comprises all possible codon dimer (dicodon) combinations.

121. The method of claim 109, wherein the library of oligonucleotides consists of 4096 codon dimer (dicodon) combinations.

122. The library of claim 109, wherein the oligonucleotide library members are between about 100 and 150 base pairs in length.

123. The method of claim 122, wherein the codons are not stop codons.

124. The method of claim 109, wherein the substrate surface comprises a solid surface.

125. The method of claim 109, wherein the substrate surface comprises a bead.

126. The method of claim 109, wherein the substrate surface comprises a polystyrene.

127. The method of claim 109, wherein the substrate surface comprises a glass.

128. The method of claim 109, wherein the substrate surface comprises a double-orificed container.

129. The method of claim 128, wherein the double-orificed container comprises a double-orificed capillary array.

130. The method of claim 129, wherein the double-orificed capillary array is a GIGAMATRIX™ capillary array.

131. The method of claim 109, wherein the substrate surface of step (b) further comprises an immobilized double-stranded oligonucleotide.

132. The method of claim 131, wherein the immobilized double-stranded oligonucleotide further comprises a codon building block oligonucleotide library member, wherein the library of oligonucleotides comprises dicodon building blocks, the library comprising a plurality of double-stranded oligonucleotide members, wherein each oligonucleotide member comprises two codons in tandem (a dicodon) and a Type-IIS restriction endonuclease recognition sequence flanking the 5' and the 3' end of the dicodon

133. The method of claim 132, wherein the codon building block oligonucleotide library member is immobilized to the immobilized double-stranded oligonucleotide by blunt end ligation.

134. The method of claim 131, wherein the immobilized double-stranded oligonucleotide comprises a single-stranded base overhang at the non-immobilized end of the oligonucleotide.

135. The method of claim 132, wherein the oligonucleotide library member is immobilized to the immobilized double-stranded oligonucleotide by base pairing of single stranded base overhangs followed by ligation.

136. The method of claim 132, wherein the Type-IIS restriction endonuclease recognition sequence at the 5' end of the dicodon differs from the Type-IIS restriction endonuclease recognition sequence at the 3' end of the dicodon.

137. The method of claim 132, wherein the Type-IIS restriction endonuclease upon digestion of the oligonucleotide library member generates a three base single-stranded overhang.

138. The method of claim 137, wherein the Type-IIS restriction endonuclease comprises a SapI restriction endonuclease or an isochizomer thereof.

139. The method of claim 137, wherein the Type-IIS restriction endonuclease comprises an EarI restriction endonuclease or an isochizomer thereof.

140. The method of claim 132, wherein the Type-IIS restriction endonuclease upon digestion of the oligonucleotide library member generates a two base single-stranded overhang.

141. The method of claim 140, wherein the Type-IIS restriction endonuclease is selected from the group consisting of BseRI, BsgI and BpmI.

142. The method of claim 132, wherein the Type-IIS restriction endonuclease upon digestion of the oligonucleotide library member generates a one base single-stranded overhang.

143. The method of claim 142, wherein the Type-IIS restriction endonuclease is selected from the group consisting of N.AlwI and N.BstNBI.

144. The method of claim 132, wherein the Type-IIS restriction endonuclease upon digestion of the oligonucleotide library member cuts on both sides of the Type-IIS restriction endonuclease recognition sequence.

145. The method of claim 144, wherein the Type-IIS restriction endonuclease is selected from the group consisting of BcgI, BsaXI and BspCNI.

146. The method of claim 132, wherein each library member consists essentially of two codons in tandem (a dicodon) and a Type-IIS restriction endonuclease recognition sequence flanking the 5' and the 3' end of the dicodon.

147. The method of claim 132, wherein the oligonucleotide library members are between about 20 and 400 base pairs in length.

148. The method of claim 147, wherein the library members are between about 40 and 200 base pairs in length.

149. The method of claim 148, wherein the library members are between about 100 and 150 base pairs in length.

150. The method of claim 132, wherein an oligonucleotide library member comprises a sequence

(NNN)(NNN) AGAAGAGC (SEQ ID NO:1)

(NNN)(NNN) TCTTCTCG (SEQ ID NO:2)

wherein (NNN) is a codon and N is A, C, T or G or an equivalent thereof.

151. The method of claim 132, wherein an oligonucleotide library member comprises a sequence

(NNN)(NNN) TGAAGAGAG (SEQ ID NO:3)

(NNN)(NNN) ACTTCTCTC (SEQ ID NO:4)

wherein (NNN) is a codon and N is A, C, T or G or an equivalent thereof.

152. The method of claim 132, wherein an oligonucleotide library member comprises a sequence

(NNN)(NNN) TGAAGAGAG CT GCTACTAACT GCA (SEQ ID NO:5)

(NNN)(NNN) ACTTCTCTC GA CGATGATTG (SEQ ID NO:6)

wherein (NNN) is a codon and N is A, C, T or G or an equivalent thereof.

153. The method of claim 132, wherein an oligonucleotide library member comprises a sequence

CTCTCTTCA NNN NNN AGAAGAGC (SEQ ID NO:7)

GAGAGAAGT NNN NNN TCTTCTCG (SEQ ID NO:8)

wherein (NNN) is a codon and N is A, C, T or G or an equivalent thereof.

154. The method of claim 132, wherein an oligonucleotide library member comprises a sequence

CTCTCTTCA NNN NNN AGAAGAGC GGGTCTTCCAACTAGAGAATTCGATATCTGCA (SEQ ID NO:9)

GAGAGAAGT NNN NNN TCTTCTCG CCCAGAAGGTTGATCTCTTAAGCTATAG (SEQ ID NO:10)

wherein (NNN) is a codon and N is A, C, T or G or an equivalent thereof.

155. The method of claim 132, wherein the immobilized double-stranded oligonucleotide comprises a general formula

$(Y)_n$ (promoter) (restriction site)(single stranded overhang)

wherein Y is any nucleotide base and n is an integer between 2 and 50.

156. The method of claim 155, wherein the promoter is selected from the group consisting of a T6 promoter, a T3 promoter and an SP6 promoter.

157. The method of claim 132, wherein an immobilized double-stranded oligonucleotide comprises a sequence

(NNN) (NNN) CGCGCG(Y)$_n$CGAATTGGAGCTC (SEQ ID NO:11)

(NNN) (NNN) GCGCGC(Y)$_n$GCTTAACCTCGAGCCCC (SEQ ID NO:12),

wherein n is an integer greater than or equal to 1, Y is any nucleoside and (NNN) is a codon.

158. The method of claim 132, wherein an immobilized double-stranded oligonucleotide comprises a sequence

(NNN) (NNN) CGCGCGTAATACGACTCACTATAGGGCGAATTGGAGCTC (SEQ ID NO:13)

(NNN) (NNN) GCGCGCATTATGCTGAGTGATATCCCGCTTAACCTCGAGCCCC (SEQ ID NO:14).

159. The method of claim 131, wherein the immobilized double-stranded oligonucleotide comprises a promoter.

160. The method of claim 159, wherein the promoter comprises a bacteriophage promoter.

161. The method of claim 160, wherein the bacteriophage promoter is a T7 promoter.

162. The method of claim 160, wherein the bacteriophage promoter is selected from the group consisting of a T6 promoter and an SP6 promoter.

163. The method of claim 135, wherein ligating the oligonucleotides comprises use of a ligase.

164. The method of claim 163, wherein ligase is selected from the group consisting of a T4 ligase and an E. coli ligase.

165. The method of claim 109, further comprising sequencing the built polynucleotide.

166. The method of claim 165, further comprising determining whether all or part of the polynucleotide sequence encodes a peptide or a polypeptide.

167. The method of claim 165, further comprising isolating the polynucleotide.

168. The method of claim 109, further comprising polymerase-based amplification of the built polynucleotide.

169. The method of claim 168, wherein the polymerase-based amplification is a polymerase chain reaction (PCR).

170. The method of claim 109, further comprising transcription of the built polynucleotide.

171. The method of claim 109, wherein the substrate comprises a double-orificed container.

172. The method of claim 171, wherein the double-orificed container comprises a double-orificed capillary array.

173. The method of claim 172, wherein the double-orificed capillary array is a GIGAMATRIX™ capillary array.

174. A multiplexed system for building a polynucleotide comprising codons by iterative assembly of codon building blocks comprising the following components:

(a) a library comprising oligonucleotide members as set forth in claim 1; and

(b) a substrate surface comprising a plurality of oligonucleotide library members of step (a) immobilized to the substrate surface.

175. The multiplexed system of claim 174, wherein the substrate surface further comprises a double-orificed capillary array.

176. The multiplexed system of claim 174, wherein the double-orificed capillary array comprises a GIGAMATRIX™ capillary array.

177. The multiplexed system of claim 174, further comprising instructions comprising a method as set forth in claim 109.

178. A library of chimeric nucleic acids encoding a plurality of chimeric antigen binding polypeptides, the library made by a method comprising the following steps:

(a) providing a plurality of nucleic acids encoding a lambda light chain variable region polypeptide domain (V_λ) or a kappa light chain variable region polypeptide domain (V_κ);

(b) providing a plurality of oligonucleotides encoding a J region polypeptide domain (V_J);

(c) providing a plurality of nucleic acids encoding a lambda light chain constant region polypeptide domain (C_λ) or a kappa light chain constant region polypeptide domain (C_κ);

(d) joining together a nucleic acid of step (a), a nucleic acid of step (c) and an oligonucleotide of step (b), wherein the oligonucleotide of step (b) is placed between the nucleic acids of step (a) and step (c) to generate a V-J-C chimeric nucleic acid coding sequence encoding a chimeric antigen binding polypeptide, and repeating this joining step to generate a library of chimeric nucleic acid coding sequences encoding a library of chimeric antigen binding polypeptides.

179. The library of claim 178, wherein an antigen binding polypeptide comprises an single chain antibody.

180. The library of claim 178, wherein an antigen binding polypeptide comprises a Fab fragment, an Fd fragment or an antigen binding complementarity determining region (CDR).

181. The library of claim 178, wherein the lambda light chain variable region polypeptide domain (Vλ) nucleic acid coding sequence or the kappa light chain variable region polypeptide domain (Vκ) nucleic acid coding sequence of step (a) are generated by an amplification reaction.

182. The library of claim 178, wherein lambda light chain constant region polypeptide domain (Cλ) nucleic acid coding sequence or the kappa light chain constant region polypeptide domain (Cκ) nucleic acid coding sequence of step (c) are generated by an amplification reaction.

183. The library of claim 181 or 182, wherein the amplification reaction comprises a polymerase chain reaction (PCR) amplification reaction using a pair of oligonucleotide primers.

184. The library of claim 183, wherein the oligonucleotide primers further comprise a restriction enzyme site.

185. The library of claim 178, wherein the lambda light chain variable region polypeptide domain (Vλ) nucleic acid coding sequence, the kappa light chain variable region polypeptide domain (Vκ) nucleic acid coding sequence, the lambda light chain constant region polypeptide domain (Cλ) nucleic acid coding sequence or the kappa light chain constant region polypeptide domain (Cκ) nucleic acid coding sequence is between about 99 and about 600 base pair residues in length.

186. The library of claim 185, wherein a nucleic acid coding sequence is between about 198 and about 402 base pair residues in length.

187. The library of claim 186, wherein a nucleic acid coding sequence is between about 300 and about 320 base pair residues in length.

188. The library of claim 181 or 182, wherein amplified nucleic acid is a mammalian nucleic acid.

189. The library of claim 188, wherein the amplified mammalian nucleic acid is a human nucleic acid.

190. The library of claim 181 or claim 182, wherein amplified nucleic acid is a genomic DNA, a cDNA or an RNA.

191. The library of claim 178, wherein an oligonucleotide encoding a J region polypeptide domain of step (b) is between about 9 and about 99 base pair residues in length.

192. The library of claim 191, wherein an oligonucleotide encoding a J region polypeptide domain of step (b) is between about 18 and about 81 base pair residues in length.

193. The library of claim 192, wherein an oligonucleotide encoding a J region polypeptide domain of step (b) is between about 36 and about 63 base pair residues in length.

194. The library of claim 178, wherein the joining of step (d) to generate a chimeric nucleic acid comprises a DNA ligase, a transcription or an amplification reaction.

195. The library of claim 194, wherein the amplification reaction comprises a polymerase chain reaction (PCR) amplification reaction.

196. The library of claim 195, wherein the amplification reaction comprises use of oligonucleotide primers.

197. The library of claim 196, wherein the oligonucleotide primers further comprise a restriction enzyme site.

198. The library of claim 194, wherein the transcription comprises a DNA polymerase transcription reaction.

199. A library of chimeric nucleic acids encoding a plurality of chimeric antigen binding polypeptides, the library made by a method comprising the following steps:

(a) providing a plurality of nucleic acids encoding an antibody heavy chain variable region polypeptide domain (V_H);

(b) providing a plurality of oligonucleotides encoding a D region polypeptide domain (V_D);

(c) providing a plurality of oligonucleotides encoding a J region polypeptide domain (V_J);

(d) providing a plurality of nucleic acids encoding a heavy chain constant region polypeptide domain (C_H);

(e) joining together a nucleic acid of step (a), a nucleic acid of step (d) and an oligonucleotide of step (b) and step (c), wherein the oligonucleotides of step (b) and step (c) are placed between the nucleic acids of step (a) and step (d) to generate a V-D-J-C chimeric nucleic acid coding sequence encoding a chimeric antigen binding polypeptide, and repeating this joining step to generate a library of chimeric nucleic acid coding sequences encoding a library of chimeric antigen binding polypeptides.

200. The library of claim 199, wherein an antigen binding polypeptide comprises an single chain antibody.

201. The library of claim 199, wherein an antigen binding polypeptide comprises a Fab fragment, an Fd fragment or an antigen binding complementarity determining region (CDR).

202. The library of claim 200 or claim 201, wherein an antigen binding polypeptide comprise a μ, γ, γ2, γ3, γ4, δ, ε, α1 or α2 constant region.

203. The library of claim 199, wherein the heavy chain variable region polypeptide domain (V_H) is generated by an amplification reaction.

204. The library of claim 199, wherein heavy chain constant region polypeptide domain (C_H) nucleic acid coding sequence is generated by an amplification reaction.

205. The library of claim 203 or claim 204, wherein the amplification reaction comprises a polymerase chain reaction (PCR) amplification reaction using a pair of oligonucleotide primers.

206. The library of claim 205, wherein the oligonucleotide primers further comprise a restriction enzyme site.

207. The library of claim 199, wherein the heavy chain variable region polypeptide domain (V_H) nucleic acid coding sequence or the heavy chain constant region polypeptide domain (C_H) nucleic acid coding sequence is between about 99 and about 600 base pair residues in length.

208. The library of claim 207, wherein a nucleic acid coding sequence is between about 198 and about 402 base pair residues in length.

209. The library of claim 208, wherein a nucleic acid coding sequence is between about 300 and about 320 base pair residues in length.

210. The library of claim 203 or claim 204, wherein amplified nucleic acid is a mammalian nucleic acid.

211. The library of claim 210, wherein the amplified mammalian nucleic acid is a human nucleic acid.

212. The library of claim 203 or claim 204, wherein amplified nucleic acid is a genomic DNA, a cDNA or an RNA.

213. The library of claim 199, wherein an oligonucleotide encoding a D region polypeptide domain of step (b) or a J region polypeptide domain of step (c) is between about 9 and about 99 base pair residues in length.

214. The library of claim 213, wherein the oligonucleotide is between about 18 and about 81 base pair residues in length.

215. The library of claim 214, wherein the oligonucleotide is between about 36 and about 63 base pair residues in length.

216. The library of claim 199, wherein the joining of step (e) to generate a chimeric nucleic acid comprises a DNA ligase, a transcription or an amplification reaction.

217. The library of claim 216, wherein the amplification reaction comprises a polymerase chain reaction (PCR) amplification reaction.

218. The library of claim 216, wherein the amplification reaction comprises use of oligonucleotide primers.

219. The library of claim 218, wherein the oligonucleotide primers further comprise a restriction enzyme site.

220. The library of claim 216, wherein the transcription comprises a DNA polymerase transcription reaction.

221. An expression vector comprising a chimeric nucleic acid selected from a library as set forth in claim 78 or claim 199.

222. A transformed cell comprising a chimeric nucleic acid selected from a library as set forth in claim 78 or claim 199.

223. A transformed cell comprising an expression vector as set forth in claim 221.

224. A non-human transgenic animal comprising a chimeric nucleic acid selected from a library as set forth in claim 78 or claim 99.

225. A method for making a chimeric antigen binding polypeptide comprising the following steps:

(a) providing a nucleic acid encoding a lambda light chain variable region polypeptide domain (V_λ) or a kappa light chain variable region polypeptide domain (V_κ);

(b) providing an oligonucleotides encoding a J region polypeptide domain (V_J);

(c) providing a nucleic acid encoding a lambda light chain constant region polypeptide domain (C_λ) or a kappa light chain constant region polypeptide domain (C_κ);

(d) joining together a nucleic acid of step (a), a nucleic acid of step (c) and an oligonucleotide of step (b), wherein the oligonucleotide of step (b) is placed between the nucleic acids of step (a) and step (c) to generate a V-J-C chimeric nucleic acid coding sequence encoding a chimeric antigen binding polypeptide.

226. A method for making a library of chimeric antigen binding polypeptides comprising the following steps:

(a) providing a plurality of nucleic acids encoding a lambda light chain variable region polypeptide domain (V_λ) or a kappa light chain variable region polypeptide domain (V_κ);

(b) providing a plurality of oligonucleotides encoding a J region polypeptide domain (V_J);

(c) providing a plurality of nucleic acids encoding a lambda light chain constant region polypeptide domain (C_λ) or a kappa light chain constant region polypeptide domain (C_κ);

(d) joining together a nucleic acid of step (a), a nucleic acid of step (c) and an oligonucleotide of step (b), wherein the oligonucleotide of step (b) is placed between the nucleic acids of step (a) and step (c) to generate a V-J-C chimeric nucleic acid coding sequence encoding a chimeric antigen binding polypeptide, and repeating this joining step to generate a library of chimeric nucleic acid coding sequences encoding a library of chimeric antigen binding polypeptides.

227. A method for making a chimeric antigen binding polypeptide comprising the following steps:

(a) providing a nucleic acid encoding an antibody heavy chain variable region polypeptide domain (V_H);

(b) providing an oligonucleotide encoding a D region polypeptide domain (V_D);

(c) providing an oligonucleotide encoding a J region polypeptide domain (V_J);

(d) providing a nucleic acid encoding a heavy chain constant region polypeptide domain (C_H);

(e) joining together a nucleic acid of step (a), a nucleic acid of step (d) and an oligonucleotide of step (b) and step (c), wherein the oligonucleotides of step (b) and step (c) are placed between the nucleic acids of step (a) and step (d) to generate a V-D-J-C chimeric nucleic acid coding sequence encoding a chimeric antigen binding polypeptide.

228. A method for making a library of chimeric antigen binding polypeptides comprising the following steps:

(a) providing a plurality of nucleic acids encoding an antibody heavy chain variable region polypeptide domain (V_H);

(b) providing a plurality of oligonucleotides encoding a D region polypeptide domain (V_D);

(c) providing a plurality of oligonucleotides encoding a J region polypeptide domain (V_J);

(d) providing a plurality of nucleic acids encoding a heavy chain constant region polypeptide domain (C_H);

(e) joining together a nucleic acid of step (a), a nucleic acid of step (d) and an oligonucleotide of step (b) and step (c), wherein the oligonucleotides of step (b) and step (c) are placed between the nucleic acids of step (a) and step (d) to generate a V-D-J-C chimeric nucleic acid coding sequence encoding a chimeric antigen binding polypeptide, and repeating this joining step to generate a library of chimeric nucleic acid coding sequences encoding a library of chimeric antigen binding polypeptides

229. The method of claim 225, 226, 227 or 228, further comprising screening the expressed chimeric antigen binding polypeptide for its ability to specifically bind an antigen.

230. The method of claim 225, 226, 227 or 228, further comprising mutagenizing the nucleic acid coding sequence encoding a chimeric antigen binding polypeptide.

231. The method of claim 230, wherein the nucleic acid is mutagenized by a method comprising an optimized directed evolution system or a synthetic ligation reassembly, or a combination thereof.

232. The method of claim 230, wherein the nucleic acid is mutagenized by a method comprising gene site saturated mutagenesis (GSSM), step-wise nucleic acid

reassembly, error-prone PCR, shuffling, oligonucleotide-directed mutagenesis, assembly PCR, sexual PCR mutagenesis, in vivo mutagenesis, cassette mutagenesis, recursive ensemble mutagenesis, exponential ensemble mutagenesis, site-specific mutagenesis, gene reassembly, synthetic ligation reassembly (SLR) or a combination thereof.

233. The method of claim 230, wherein the nucleic acid is mutagenized by a method comprising recombination, recursive sequence recombination, phosphothioate-modified DNA mutagenesis, uracil-containing template mutagenesis, gapped duplex mutagenesis, point mismatch repair mutagenesis, repair-deficient host strain mutagenesis, chemical mutagenesis, radiogenic mutagenesis, deletion mutagenesis, restriction-selection mutagenesis, restriction-purification mutagenesis, artificial gene synthesis, ensemble mutagenesis, chimeric nucleic acid multimer creation or a combination thereof.

234. The method of claim 230, further comprising screening the mutagenized chimeric antigen binding polypeptide for its ability to specifically bind an antigen.

235. The method of claim 229 or claim 234, comprising identifying an antigen binding site variant by its increased antigen binding affinity or antigen binding specificity as compared to the affinity or specificity of the chimeric antigen binding polypeptide before mutagenesis.

236. The method of claim 229 or claim 234, comprising screening the antigen binding polypeptide for its ability to specifically bind an antigen by a method comprising phage display of the antigen binding site polypeptide.

237. The method of claim 229 or claim 234, comprising screening the antigen binding polypeptide for its ability to specifically bind an antigen by a method comprising expression of the expressed antigen binding site polypeptide in a liquid phase.

238. The method of claim 229 or claim 234, comprising screening the antigen binding polypeptide for its ability to specifically bind an antigen by a method comprising ribosome display of the antigen binding site polypeptide.

239. The method of claim 225, 226, 227 or 228, further comprising screening the chimeric antigen binding polypeptide for its ability to specifically bind an antigen by a method comprising immobilizing the polypeptide in a solid phase.

240. The method of claim 239, comprising screening the chimeric antigen binding polypeptide for its ability to specifically bind an antigen by a method comprising a capillary array.

241. The method of claim 240, comprising screening the chimeric antigen binding polypeptide for its ability to specifically bind an antigen by a method comprising a double-orificed container.

242. The method of claim 241, wherein the double-orificed container comprises a double-orificed capillary array.

243. The method of claim 242, wherein the double-orificed capillary array is a GIGAMATRIX™ capillary array.

244. A method for making a library of chimeric antigen binding polypeptides comprising the following steps:

(a) providing a plurality of V-J-C chimeric nucleic acids encoding a chimeric antigen binding polypeptide made by a method as set forth in claim 48 or a plurality of V-D-J-C chimeric nucleic acids encoding a chimeric antigen binding polypeptide made by a method as set forth in claim 50;

(b) providing a plurality of oligonucleotides, wherein each oligonucleotide comprises a sequence homologous to a chimeric nucleic acid of step (a), thereby targeting a specific sequence of the chimeric nucleic acid, and a sequence that is a variant of the

chimeric nucleic acid; and

(c) generating "n" number of progeny polynucleotides comprising non-stochastic sequence variations by replicating the chimeric nucleic acid of step (a) with the oligonucleotides of step (b), wherein n is an integer, thereby generating a library of chimeric antigen binding polypeptides.

245. The method of claim 244, wherein the sequence homologous to the chimeric nucleic acid is x bases long, wherein x is an integer between 3 and 100.

246. The method of claim 245, wherein, wherein the sequence homologous to the chimeric nucleic acid is x bases long, wherein x is an integer between 5 and 50.

247. The method of claim 246, wherein, wherein the sequence homologous to the chimeric nucleic acid is x bases long, wherein x is an integer between 10 and 30.

248. The method of claim 244, wherein, the sequence that is a variant of the chimeric nucleic acid is x bases long, wherein x is an integer between 1 and 50.

249. The method of claim 248, wherein, wherein the sequence that is a variant of the chimeric nucleic acid is x bases long, wherein x is an integer between 2 and 20.

250. The method of claim 244, wherein the oligonucleotide of step (b) further comprises a second sequence homologous to the chimeric nucleic acid and the variant sequence is flanked by the sequences homologous to the chimeric nucleic acid.

251. The method of claim 250, wherein the second sequence that is a variant of the chimeric nucleic acid is x bases long, wherein x is an integer between 1 and 50.

252. The method of claim 250, wherein the second sequence is x bases long, wherein x is 3, 6, 9 or 12.

253. The method of claim 244, wherein the oligonucleotides comprise variant sequences targeting a chimeric nucleic acid codon, thereby generating a plurality of progeny chimeric polynucleotides comprising a plurality of variant codons.

254. The method of claim 244, wherein the variant sequences generate variant codons encoding all nineteen naturally-occurring amino acid variants for a targeted codon, thereby generating all nineteen possible natural amino acid variations at the residue encoded by the targeted codon.

255. The method of claim 244, wherein the oligonucleotides comprise variant sequences targeting a plurality of chimeric nucleic acid codons.

256. The method of claim 244, wherein the oligonucleotides comprising variant sequences target all of the codons in the chimeric nucleic acid, thereby generating a plurality of progeny polypeptides wherein all amino acids are non-stochastic variants of the polypeptide encoded by the chimeric nucleic acid.

257. The method of claim 244, wherein the variant sequences generate variant codons encoding all nineteen naturally-occurring amino acid variants for all of the chimeric nucleic acid codons, thereby generating a plurality of progeny polypeptides wherein all amino acids are non-stochastic variants of the polypeptide encoded by the chimeric nucleic acid and a variant for all nineteen possible natural amino acids at all of the codons.

258. The method of claim 244, wherein the n is an integer between 1 and about 10^{30}.

259. The method of claim 258, wherein the n is an integer between about 10^{2} and about 10^{20}.

260. The method of claim 259, wherein the n is an integer between about 10^{2} and about 10^{10}.

261. The method of claim 244, wherein the replicating of step (c) comprises an enzyme-based replication.

262. The method of claim 261, wherein the enzyme-based replication comprises a polymerase-based amplification reaction.

263. The method of claim 262, wherein the amplification reaction comprises a polymerase chain reaction (PCR).

264. The method of claim 263, wherein the enzyme-based replication comprises an error-free polymerase reaction.

265. The method of claim 244, wherein an oligonucleotide of step (b) further comprises a nucleic acid sequence capable of introducing one or more nucleotide residues into the template polynucleotide.

266. The method of claim 265, wherein an oligonucleotide of step (b) further comprises a nucleic acid sequence capable of deleting one or more residue from the template polynucleotide.

267. The method of claim 266, wherein the oligonucleotide of step (b) further comprises addition of one or more stop codons to the template polynucleotide.

268. A method for making a library of chimeric antigen binding polypeptides comprising the following steps:

(a) providing (i) x number of V-J-C chimeric nucleic acids encoding a chimeric antigen binding polypeptide made by a method comprising providing a nucleic acid encoding a lambda light chain variable region polypeptide domain (Vλ) or a kappa light chain variable region polypeptide domain (Vκ); providing an oligonucleotides encoding a J region polypeptide domain (VJ); providing a nucleic acid encoding a lambda light chain

constant region polypeptide domain (Cλ) or a kappa light chain constant region polypeptide domain (Cκ); and joining together a nucleic acid of step (a), a nucleic acid of step (c) and an oligonucleotide of step (b), wherein the oligonucleotide of step (b) is placed between the nucleic acids of step (a) and step (c) to generate a V-J-C chimeric nucleic acid coding sequence encoding a chimeric antigen binding polypeptide; or, (ii) x number of V-D-J-C chimeric nucleic acids encoding a chimeric antigen binding polypeptide made by a method comprising providing a nucleic acid encoding an antibody heavy chain variable region polypeptide domain (VH); providing an oligonucleotide encoding a D region polypeptide domain (VD); providing an oligonucleotide encoding a J region polypeptide domain (VJ); (d) providing a nucleic acid encoding a heavy chain constant region polypeptide domain (CH); and, joining together a nucleic acid of step (a), a nucleic acid of step (d) and an oligonucleotide of step (b) and step (c), wherein the oligonucleotides of step (b) and step (c) are placed between the nucleic acids of step (a) and step (d) to generate a V-D-J-C chimeric nucleic acid coding sequence encoding a chimeric antigen binding polypeptide;

(b) providing y number of building block polynucleotides, wherein y is an integer, and the building block polynucleotides are designed to cross-over reassemble with a chimeric nucleic acid of step (a) at predetermined sequences and comprise a sequence that is a variant of the chimeric nucleic acid and a sequence homologous to the chimeric nucleic acid flanking the variant sequence; and,

(c) combining at least one building block polynucleotide with at least one chimeric nucleic acid such that the building block polynucleotide cross-over reassembles with the chimeric nucleic acid to generate non-stochastic progeny chimeric polynucleotides, thereby generating a library of polynucleotides encoding chimeric antigen binding polypeptides.

269. The method of claim 268, wherein x is an integer between 1 and about 10^{10}.

270. The method of claim 269, wherein the x is an integer between about 10 and about 10^2.

271. The method of claim 268, wherein the x is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10.

272. The method of claim 268, wherein a plurality of building block polynucleotides are used and the variant sequences target a chimeric nucleic acid codon to generate a plurality of progeny polynucleotides that are variants of the targeted codon, thereby generating a plurality of natural amino acid variations at a residue in a polypeptide encoded by the chimeric nucleic acid.

273. The method of claim 272, wherein the variant sequences generate variant codons encoding all nineteen naturally-occurring amino acid variants for the targeted codon, thereby generating all nineteen possible natural amino acid variations at the residue encoded by the targeted codon in a polypeptide encoded by the chimeric nucleic acid.

274. The method of claim 268, wherein a plurality of building block polynucleotides are used, and the variant sequences target a plurality of chimeric nucleic acid codons, thereby generating a plurality of codons that are variants of the targeted codons and a plurality of natural amino acid variations at a plurality of residues encoded by the targeted codon in a polypeptide encoded by the chimeric nucleic acid.

275. The method of claim 274, wherein the variant sequences generate variant codons in all of the codons in the chimeric nucleic acid, thereby generating a plurality of progeny polypeptides wherein all amino acids are non-stochastic variants of the polypeptide encoded by the chimeric nucleic acid.

276. The method of claim 275, wherein the variant sequences generate variant codons encoding all nineteen naturally-occurring amino acid variants for all of the chimeric nucleic acid codons, thereby generating a plurality of progeny polypeptides wherein all amino acids are non-stochastic variants of the polypeptide encoded by the chimeric nucleic acid and a variant for all nineteen possible natural amino acids at all of the codons.

277. The method of claim 274, wherein all of the codons in an antigen binding site are targeted.

278. The method of claim 268, wherein the library comprises between 1 and about 10^{30} members.

279. The method of claim 278, wherein the library comprises between about 10^{2} and about 10^{20} members.

280. The method of claim 279, wherein the library comprises between about 10^{3} and about 10^{10} members.

281. The method of claim 268, wherein an end of a building block polynucleotide comprises at least about 6 nucleotides homologous to a chimeric nucleic acid.

282. The method of claim 281, wherein an end of a building block polynucleotide comprises at least about 15 nucleotides homologous to a chimeric nucleic acid.

283. The method of claim 282, wherein an end of a building block polynucleotide comprises at least about 21 nucleotides homologous to a chimeric nucleic acid.

284. The method of claim 268, wherein combining one or more building block polynucleotides with a chimeric nucleic acid comprises z cross-over events between the building block polynucleotides and the chimeric nucleic acid, wherein y is an integer between 1 and about 10^{20}.

285. The method of claim 284, wherein z is an integer between about 10 and about 10^{10}.

286. The method of claim 284, wherein z is an integer between about 10^2 and about 10^5.

287. The method of claim 268, wherein a non-stochastic progeny chimeric polynucleotide differs from a chimeric nucleic acid in z number of residues, wherein z is between 1 and about 10^4.

288. The method of claim 287, wherein a non-stochastic progeny chimeric polynucleotide differs from the template polynucleotide in z number of residues, wherein z is between 10 and about 10^3.

289. The method of claim 268, wherein a non-stochastic progeny chimeric polynucleotide differs from the template polynucleotide in z number of residues, wherein z is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10.

290. The method of claim 268, wherein a non-stochastic progeny chimeric polynucleotide differs from a chimeric nucleic acid in z number of codons, wherein z is between 1 and about 10^4.

291. The method of claim 290, wherein a non-stochastic progeny chimeric polynucleotide differs from a chimeric nucleic acid in z number of codons, wherein z is between 10 and about 10^3.

292. The method of claim 268, wherein a non-stochastic progeny chimeric polynucleotide differs from a chimeric nucleic acid in z number of codons, wherein z is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10.